Global Prevalence of Depression among Heart Failure Patients: A Systematic Review and Meta-Analysis

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Abstract: The present study aimed to evaluate the prevalence of depression among heart failure (HF) patients. Depression is one of the main risk factors of mortality and reduction in quality of life in patients with HR. Despite individual studies, there is no comprehensive study on depression in HF patients. In the present systematic review and meta-analysis, databases (Web of Science, Scopus, and PubMed) were searched from January 1, 2000, to December 15, 2020. The keywords used included: depression and heart failure. The research stages including search, screening, quality evaluation, and extraction of study data

Disclosures: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
Patient Consent: This article does not contain any studies with human or animal subjects performed by any of the authors. Availability of data and material (data transparency). Code availability (software application or custom code). Authors' contributions (optional: please review the submission guidelines from the journal whether statements are mandatory). Additional declarations for articles in life science journals that report the results of studies involving humans and/or animals. Ethics approval (include appropriate approvals or waivers). Consent to participate (include appropriate statements). Consent for publication (include appropriate statements).
Funding: None.
Curr Probl Cardiol 2022;47:100848
0146-2806/$ – see front matter
https://doi.org/10.1016/j.cpcardiol.2021.100848

were performed separately by two researchers. A total of 149 studies performed on 305,407 HF patients entered the final stage. The global prevalence of any severity and moderate to severe severity of depression was 41.9% and 28.1%, respectively. The results of the subgroup analysis showed that the prevalence of depression was higher in women (45.5%) than in men. Also, according to the NHYA classification, the prevalence of depression in patients in stages three and four (54.7%) was higher than stages 1 and 2. The prevalence of depression was higher in the EMRO region (70.1%) and lower economic status countries (56.7%). The high prevalence of depression among HF patients indicates the importance of paying more attention and providing the necessary training for patients to reduce depression. (Curr Probl Cardiol 2022;47:100848.)

Introduction

Despite advances, heart failure (HF) is still considered a growing disease. The latest results of the GBD study show that more than 64 million people worldwide suffer from HF of varying severities.[1] Unlike the physical dimension, there are few studies on the psychological dimension in most HF patients, while HF patients suffer from various psychological disorders due to prolonged exposure to the disease, use of various drugs, and poor prognosis.

One of the most prevalent psychological complications in HF patients is depression. A previous study showed that the depression prevalence among HF patients was 21.6%.[2] Depression in HF patients reduces adherence to the treatment regimen,[3] decreases adaptation to the disease[4] and ultimately causes disruption in the treatment process, and reduces the quality of life of patients.[5] Studies have also shown that depression is a major risk factor for increased mortality among HF patients.[6,7] On the other hand, depressive HF patients impose about 30% more costs on the health system.[8]

Despite the importance of depression among HF patients, there have been fewer studies on it. To the best knowledge of researchers, the last relevant systematic review and meta-analysis was carried out 16 years ago (2005)[2] and only on two databases. However, determining the updated prevalence of depression can help achieve a better understanding of its importance among health professionals and help health

policymakers plan prevention programs. The present study aimed to determine the prevalence of depression among HF patients.

Methods

Design and Registration

This systematic review and meta-analysis was performed using Cochran's book[9] and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.[10] The protocol is registered in PROPERO (CRD42021227005).

Eligibility Criteria

Cross-sectional, cohort, and RCT studies published in English language peer-reviewed journals were included in the present study. The target population was HF inpatients and/or outpatients aged > 18 years. Studies in which depression was assessed using a standard instrument or interview were included in the present study.

Search Strategy

Three international databases (Web of Science, Scopus, and PubMed) were searched from January 1, 2000 to December 15, 2020. Boolean operators (AND, OR, and NOT), Medical Subject Headings (MeSH), truncation "*" used for search in databases using the following keywords: depression and heart failure (Supplementary Table 1).

Study Selection and Data Extraction

After searching in the three databases, the articles were entered into EndNote software. The articles were then screened. Duplicate articles were initially removed. Then, the titles and abstracts of the articles were reviewed based on the inclusion criteria and irrelevant items were excluded. Then the full text of the remaining articles was evaluated and the final articles were selected. Excel software was used to extract the data. Extracted data items included: general information (author; year; Region (World Bank category), Economic status (World bank category), country); methodology information (sampling method; design; sampling method, number of sites, mode of data collection, Questioner, Design, Setting), and Participants (age, gender, New York Heart Association

(NYHA) Functional Classification (I.II, III, IV)) and main outcome (prevalence of depression).

Quality Assessment

Two different instruments were used to evaluate the methodological quality of the studies based on the type of study. To evaluate the quality of cross-sectional studies, Hoy et al. 10-item instrument evaluated the studies in terms of external and internal validity.[11] For RCT JADAD instrument was used.[12]

Data Synthesis

All the eligible studies were included in the synthesis after a systematic review. The depression prevalence assessed based-on attention to severity. So, we meta-analyzed and obtain the pooled prevalence of any severity, mild, moderate, severe, moderate-to-severe depression, and also depression based-on clinical diagnosis. In this study, depression of any severity means having depression, versus no depress. In other words, in this type of prevalence, there have been studies that have considered cut-offs to classify the existence of depression as mild or higher. Also, we meta-analyzed the mean score of depression by scales (assessment tools). The Mata-analysis was conducted, based on the random-effects model. The data and pooled prevalence were presented using the forest plot and tables. The heterogeneity of the preliminary studies was evaluated by I^2 statistic. Sub-group analysis was performed for sex, NYHA class, scales, WHO regain, economic status, and countries. The univariate meta-regression analyses were conducted for the prevalence of any severity depression prevalence. Meta-analysis was performed using STATA 14 (StataCorp, Texas, USA).

Results

Studies Information

Study Selection. A total of 8502 articles were found during searches in databases. After excluding duplicate articles, 6942 articles entered the next stage. At this stage, the articles were reviewed in terms of title and abstract, and 6753 articles were excluded due to lack of inclusion criteria. In the last stage, a total of 189 complete articles were reviewed, of which 149 articles met the inclusion criteria. The 40 excluded articles published

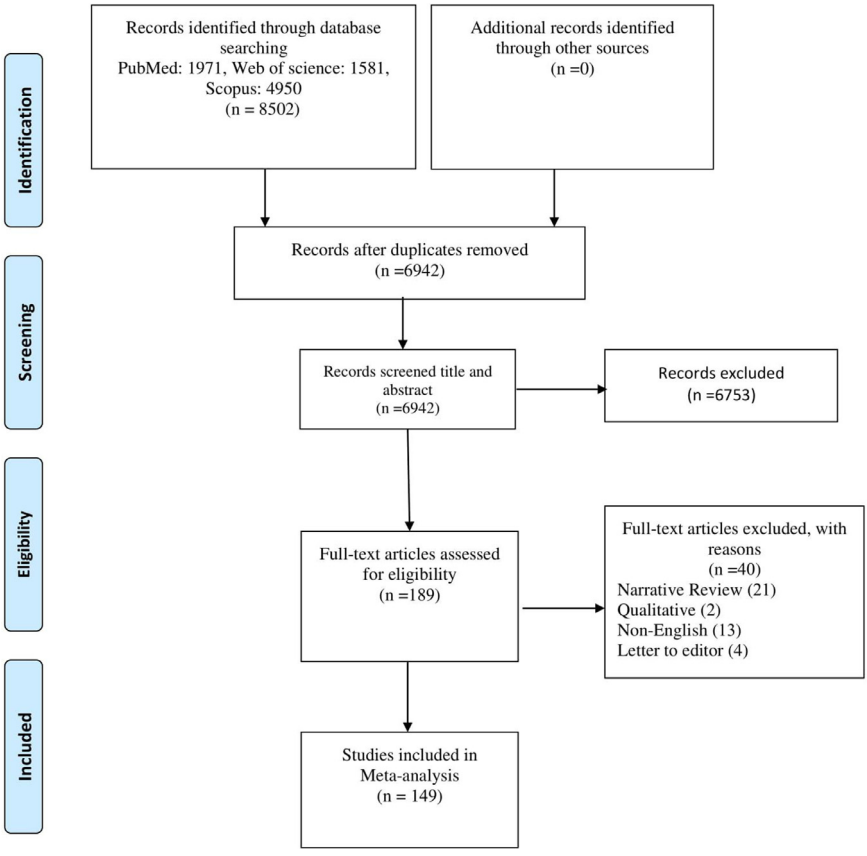


FIG 1. Study selection process. (Color version of figure is available online.)

included: Narrative Review (n = 21), Qualitative (n = 2), Non-English (n = 13), and letter to editor (n = 4) (Fig 1).

Study Characteristics. A total of 149 studies performed on 305407 HF patients over 20 years (from January 1, 2000, to December 15, 2020) entered. Most studies were conducted in the Americas (n = 70, 47.6%) and Europe continents (n = 43, 29.3%) and the United States (n = 64, 43%) and Germany (n = 13, 8.7%) countries. Majorities of studies were descriptive studies (n = 136, 91.2%) and sampling method were convenience (n = 137, 91.9%). Most studies were multicenter and prospective (n = 142). The mean age of participants was 65.2 ± 7.1 years. The number of participants was expressed by gender in 138 studies. Most of the participants were male (n = 135525). The number of patients was mentioned based on the stage of the disease in 93 studies. Out of 150,601

patients, most of them were in stages I and II of the disease (n = 97227). The studies had low bias risk and good quality. In all studies, the standard Instruments was used to assess depression. In most studies (n = 132), self-reporting was used as a common approach for gathering data. In most studies, PHQ (n = 40) and BDI (n = 38) instruments were used. Other widely used instruments included GDS (n = 13) and HADS (n = 19). In retrospective studies, depression was defined according to the ICD code. (Supplementary Table 2).

Main Results

Global Prevalence of Depression With any Severity. Of 149 included studies, 141 studies reported prevalence of depression in at-least one severity classification. The prevalence of depression based on the severity of mild, moderate, and severe, and moderate-to-severe assessed in 94 and 34 studies, respectively. Also, the prevalence was assessed based-on clinical diagnosis in 12 studies. The prevalence of depression in this study was assessed based-on 12 different tools. Most studies used the BDI (32 studies), GDS (13 studies), and PHQ-9 (13 studies) tool.

The pooled prevalence of mild depression in 5821 HF patients (n = 21) was 25.0% (95% CI: 20.2, 29.8%; I2 = 95.4%). The pooled prevalence of moderate depression in 2683 HF patients (n = 13) was 17.1% (95% CI: 11.3, 22.9; I2 = 95.3%) and the pooled prevalence of severe depression in 2726 HF patients (n = 14) was 7.2% (95% CI: 4.7, 9.6; I2 = 93.2%). Also, the pooled prevalence of depression based-on clinical diagnosis in 262815 HF patients (n = 12) was 42.0% (95% CI: 36.9, 47.1; I2 = 98.9%) (Supplementary Fig 1). The depression prevalence with any severity (in 94 study) reported between 7.5% to 100%; and the global pooled prevalence of depression in 25,591 HF patients was 41.9% (95% CI: 36.7, 47.1; I2 = 98.9%). The lowest pooled prevalence of any severity depression was for study based-on CES tool and equal 34.2% (95% CI: 26.1 to 42.3%) (Fig 2 and Supplementary Fig 2).

The prevalence of depression with any severity by sex was reported in 31 studies (of 94 study). Sub-group analysis based-on sex showed the pooled prevalence of depression with any severity in 7502 male and in 4467 females was 36.6% (95% CI: 30.3, 42.9; I2 = 97.4%) and 45.5% (95% CI: 39.2, 51.8; I2 = 94.7%), respectively (Supplementary Table 3). The pooled odds ratio of depression with any severity for sex was 1.53 (95% CI: 1.41, 1.66; I2 = 78.8%). So, the odds of depression with any

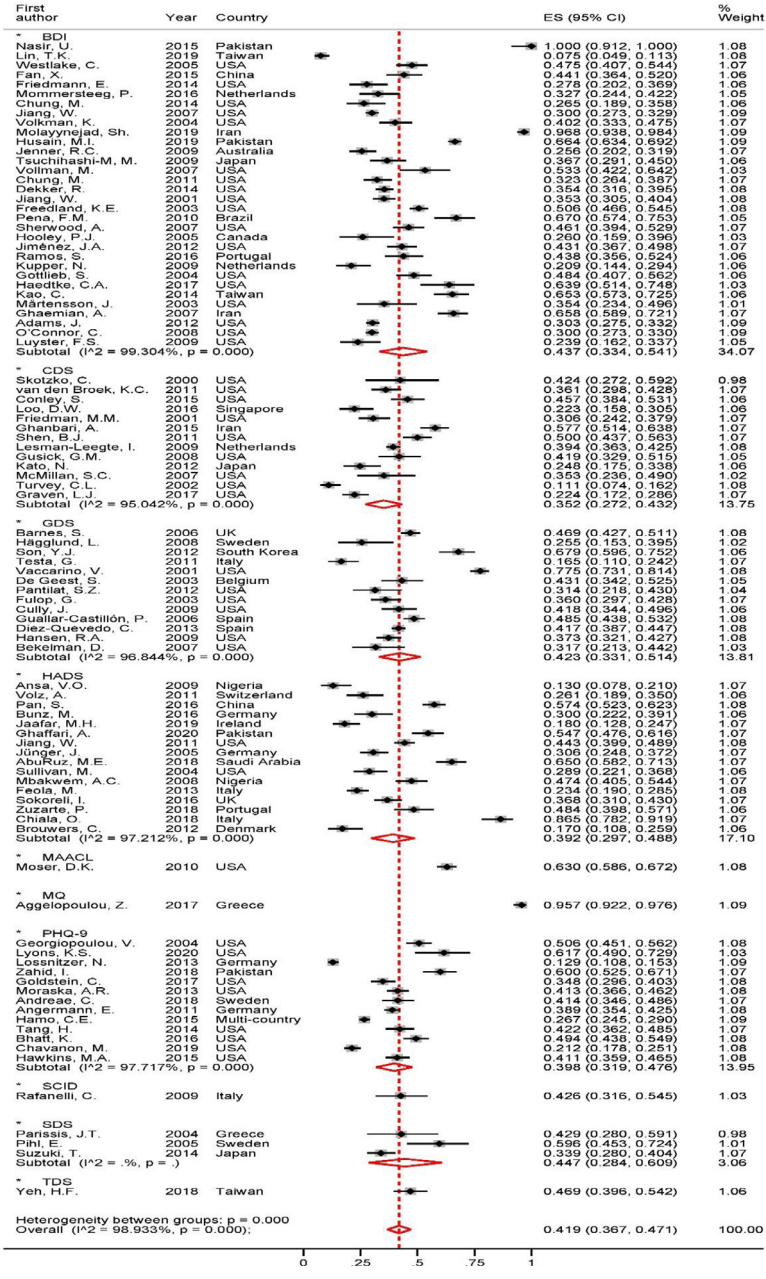
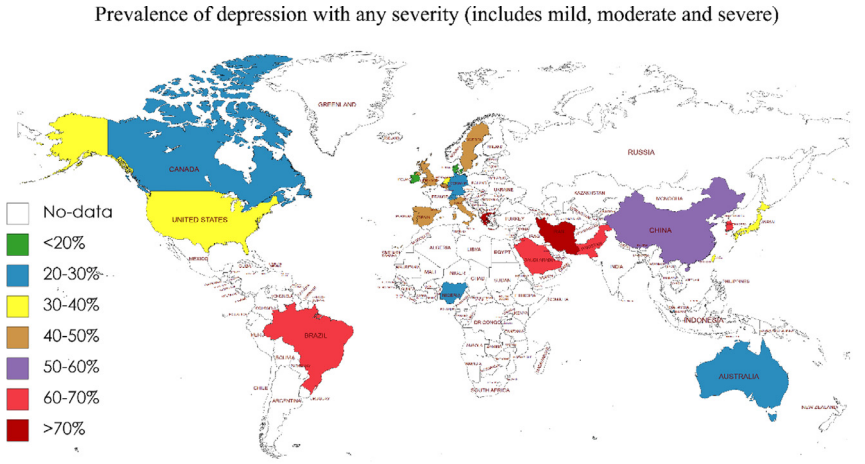


FIG 2. Global prevalence of depression any severity among HF patients based on scales. (Color version of figure is available online.)



Country	N, Ss	Pooled prevalence (95% CI)	Country	N, Ss	Pooled prevalence (95% CI)
Denmark	1, 94	22.3 (15.8, 30.5)	Taiwan	3, 588	42.2 (9.8, 74.6)
Ireland	1, 161	25.6 (20.2, 31.9)	Sweden	3, 280	43.1 (34.2, 52.5)
Singapore	1, 121	26.0 (15.9, 39.6)	Italy	4, 588	43.6 (40.1, 47.1)
Australia	1, 211	26.1 (18.9, 35.0)	Belgium	1, 109	43.7 (41.1, 46.2)
Canada	1, 50	26.7 (24.5, 29.0)	UK	2, 784	46.0 (39.9, 52.2)
Switzerland	1, 111	28.0 (12.6, 43.5)	Spain	2, 1450	53.5 (49.2, 57.8)
Multi-country	1, 1431	29.1 (24.3, 33.9)	Portugal	2, 254	65.0 (58.2, 71.3)
Germany	4, 1860	31.3 (19.5, 43.1)	China	2, 518	67.0 (57.4, 75.3)
Nigeria	2, 294	32.0 (25.5, 38.6)	Saudi Arabia	1, 200	67.9 (59.6, 75.2)
Netherlands	3, 1172	39.7 (35.5, 43.8)	Pakistan	4, 1411	70.4 (48.6, 92.2)
Japan	3, 465	39.8 (1.9, 77.7)	Iran	3, 686	73.6 (45.9, 101.3)
USA	44, 12250	41.9 (25.9, 57.9)	Greece	2, 266	94.4 (91.8, 96.9)

N: Number of studies, Ss: Sum of sample size

FIG 3. The pooled prevalence and distribution of depression with any severity in heart failure patients in the world based on countries. (Color version of figure is available online.)

severity in female HF patients was significantly 1.5 times higher than in males (Supplementary Fig 3).

Prevalence of depression with any severity was assessed in 94 studies witches conducted in 23 countries and one multi-country study. Of 23 countries, 15 countries have only one study and most studies were conducted in the United States (44 studies). The lowest and highest pooled prevalence of depression was for Denmark (22.3%) and Greece (94.4%), respectively (Fig 3). The pooled prevalence of depression in Denmark, Ireland, Singapore, Australia, Canada, Switzerland, Germany, Nigeria, Netherlands, and Japan was lower than the overall pooled prevalence (41.9%) based-on 94 studies.

Global Prevalence of Depression With Moderate-to-Severe Depression. The prevalence of moderate-to-severe depression (in 55 studies) reported between 5.6% to 55.8%. The pooled prevalence of

moderate-to-severe depression in 20,530 HF patients was 28.1% (95% CI: 24.5, 31.7; I2 = 97.5%) (Supplementary Fig 4). The prevalence of moderate-to-severe depression in this study was assessed based-on 10 different tools. Most studies used the PHQ (32 studies), BDI (7 studies), and HADS (6 studies) tool. The pooled prevalence of moderate-to-severe depression based-on PHQ, BDI and HADS tools was 29.3% (95% CI: 24.2 to 34.3%), 27.8% (95% CI: 19.0 to 36.5%) and 25.8% (95% CI: 13.1 to 38.5%), respectively (Fig 4).

The prevalence of moderate-to-severe depression by sex was reported in 8 studies (of 55 studies). Sub-group analysis based-on sex showed the pooled prevalence in 3750 male and in 2289 females was 30.1% (95% CI: 23.5, 36.7; I2 = 87.1%) and 24.4% (95% CI: 18.0, 30.9; I2 = 95.4%), respectively (Supplementary Table 4). Based-on eight study (2289 female and 3750 male), the pooled odds ratio of moderate-to-severe depression for sex was 1.34 (95% CI: 1.17, 1.52; I2 = 71.0%). So, odds of moderate-to-severe depression in female HF patients were significantly 1.34 times higher than in the male.

The prevalence of moderate-to-severe depression was assessed in 55 studies witches conducted in 20 countries and one multi-country study. Of 20 countries, 15 countries have only one study and most studies were conducted in the United States (22 studies). The lowest and highest pooled prevalence of moderate-to-severe depression was for Nigeria (11.3%) and Saudi Arabia (51.0%), respectively (Fig 5). The pooled prevalence of moderate-to-severe depression in Pakistan, Italy, Brazil, South Korea, Morocco, Ethiopia, and Saudi Arabia was higher than the overall pooled prevalence (28.1%) based-on 55 studies.

Prevalence of Depression Based on Economic Status, WHO Region, and NYHA Categories. In any severity of depression, of 94 studies, 78, 9, and 6 study conducted in high-income, upper-middle and lower-middle-income countries, respectively. Also, a multi-country study was conducted. Sub-group analysis based-on economic status showed the pooled prevalence of depression with any severity was higher in the lower-to-upper middle income [56.7% (95% CI: 39.5, 73.9)] than high income [39.2% (95% CI: 34.8, 43.7)]; and, this prevalence difference was statistically significant in 20,993 and 4598 patients in lower-to-upper middle and high-income country, respectively ($P < 0.001$) (Supplementary Fig 5). In the moderate-to-severe depression, of 55 studies, 45, 4, and 4 study conducted in high-income, upper-middle and lower-middle-income countries, respectively. Also, one study conducted on low-income countries and one in multi-country. Sub-group analysis based-on economic status

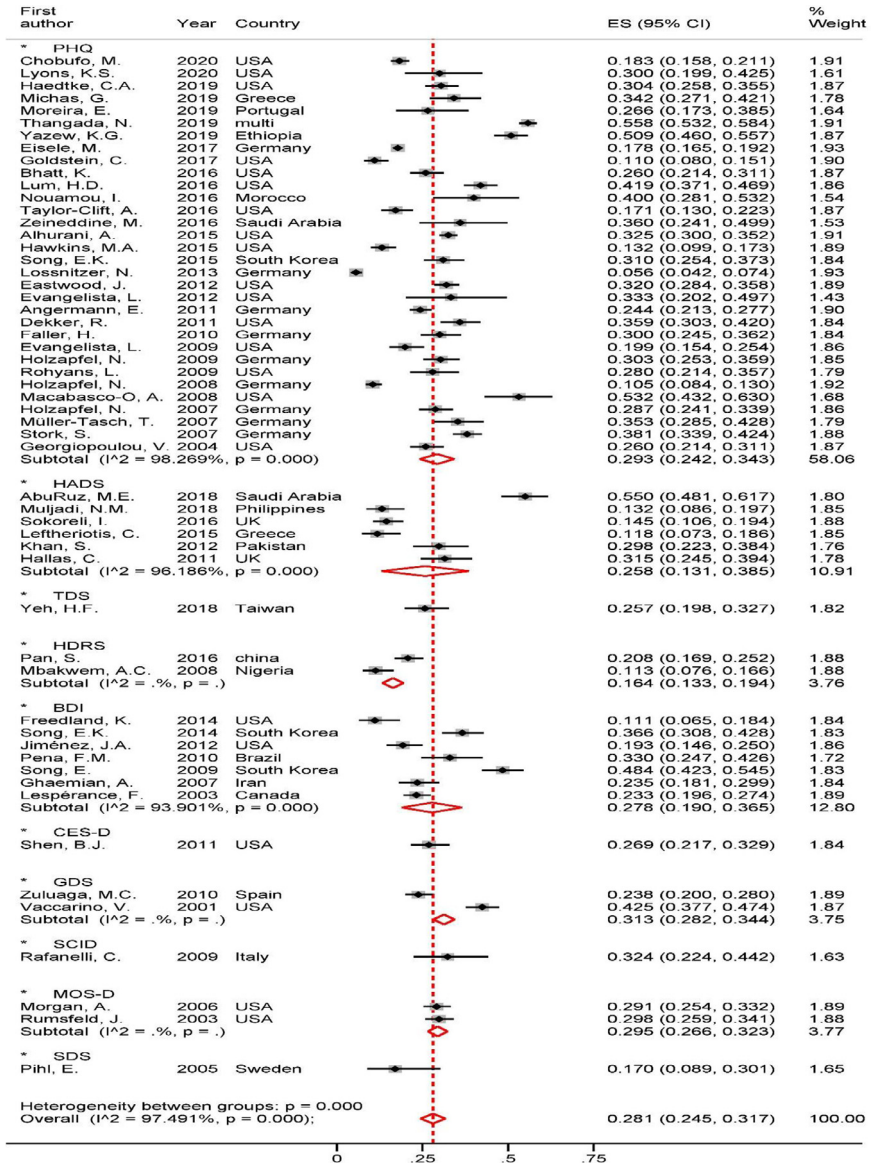
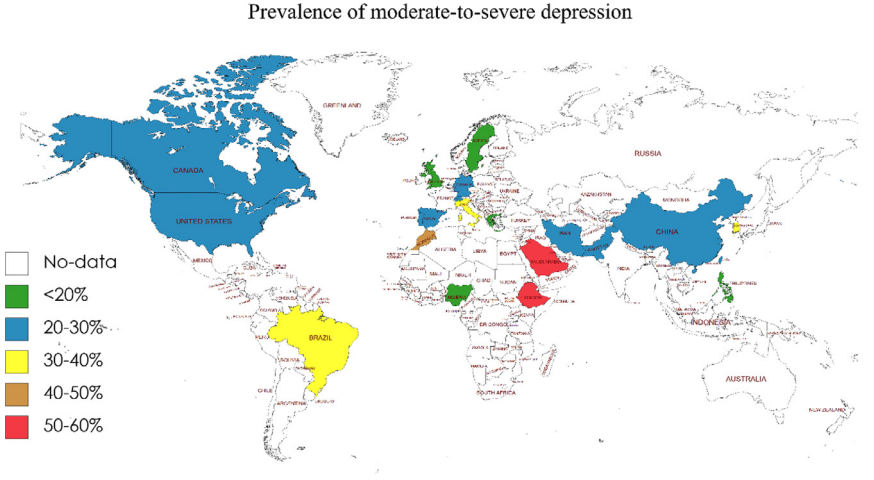


FIG 4. Global prevalence of depression with moderate-to-severe severity among HF patients based on scales. (Color version of figure is available online.)

showed pooled prevalence moderate-to-severe depression was same amount in high income [27.5% (95% CI: 24.2, 30.8)] and the no-high income (lower-to-upper middle or low income) [27.3% (95% CI: 18.0, 36.6)] (Supplementary Fig 6).



Country	N, Ss	Pooled prevalence (95% CI)	Country	N, Ss	Pooled prevalence (95% CI)
Nigeria	1, 194	11.3 (7.6, 16.6)	Portugal	1, 64	26.6 (17.3, 38.5)
Philippines	1, 144	13.2 (8.6, 19.7)	USA	22, 7698	27.2 (23.1, 31.3)
Sweden	1, 47	17.0 (8.9, 30.1)	Pakistan	1, 121	29.8 (22.3, 38.4)
UK	2, 388	18.8 (15.0, 22.7)	Italy	1, 68	32.4 (22.4, 44.2)
Greece	2, 279	19.8 (15.3, 24.3)	Brazil	1, 103	33.0 (24.7, 42.6)
China	1, 366	20.8 (16.9, 25.2)	South Korea	3, 729	38.7 (28.7, 48.7)
Canada	1, 443	23.3 (19.6, 27.4)	Morocco	1, 55	40.0 (28.1, 53.2)
Iran	1, 196	23.5 (18.1, 29.9)	Ethiopia	1, 403	50.9 (46.0, 55.7)
Spain	1, 433	23.8 (20.0, 28.0)	Saudi Arabia	2, 250	51.0 (44.9, 57.1)
Germany	9, 6943	24.2 (17.4, 31.0)	Multi-country	1, 1431	55.8 (53.2, 58.4)
Taiwan	1, 175	25.7 (19.8, 32.7)			

N: Number of studies, Ss: Sum of sample size

FIG 5. The pooled prevalence and distribution of moderate-to-severe depression in heart failure patients in the world. (Color version of figure is available online.)

In any severity depression, sub-group analysis WHO region showed pooled prevalence depression with any severity was significantly higher in the Eastern Mediterranean region [71.0% (95% CI: 57.2, 84.7)] than Americas (40.0%), Western Pacific (39.2%) and Europe (38.8%). The pooled prevalence for two studies of the Africa region was 29.1% (95% CI: 24.3, 33.9) (Supplementary Fig 7). In the moderate-to-severe depression, sub-group analysis WHO region showed pooled prevalence of moderate-to-severe depression was higher in the Eastern Mediterranean region [36.8% (95% CI: 23.4, 50.2)] than Americas (27.3%), Western Pacific (29.2%) and Europe (24.0%). The pooled prevalence for two studies of the Africa region was 29.3% (95% CI: 26.0, 32.6) (Supplementary Fig 8).

The prevalence of depression with any severity by NYHA class reported in 19 studies (of 94 study). Sub-group analysis based-on NYHA

class showed the pooled prevalence of depression with any severity in 4480 patients with NYHA class I, II and in 3034 patients with NYHA class, III, IV was 32.0% (95% CI: 25.7, 38.3; I2 = 96.1%) and 54.7% (95% CI: 41.8, 67.6; I2 = 98.6%), respectively (Supplementary Table 5). The pooled odds ratio of depression with any severity for NYHA class was 2.50 (95% CI: 2.24, 2.78; I2 = 90.3%). So, odds of depression with any severity in HF patients with NYHA class 3,4 was significantly 2.5 times higher than NYHA class 1,2 (Supplementary Fig 9).

Meta-Analysis Based-on Depression Mean Score. Depression means score reported in 71 studies based-on 18 tools. Although of them, the BDI-21 (in 21 studies), PHQ-9 (in 16 studies), and HADS-14 (in 10 studies) were used most of the other tools. Depression means score in the study with BDI-21 assessment tools reported between 6.7 to 46.5. The pooled mean score for BDI-21 in 4387 patients based-on on the random-effects model was 14.3 (95% CI: 11.2, 17.5). Depression means score in the study with PHQ-9 assessment tools reported between 4.2 to 16.4. The pooled mean score for PHQ-9 in 9,505 patients based-on on the random-effects model was 7.5 (95% CI: 5.5, 9.7). Depression means score in the study with HADS-14 assessment tools reported between 4.5 to 14.0. The pooled mean score for HADS-14 in 1887 patients based on the random-effects model was 8.0 (95% CI: 6.3, 14.1) (Supplementary Table 6).

Meta-Regression Result. The results of univariate meta-regression analysis showed publication year of study and mean age of patients was not significantly contributed to the heterogeneity of prevalence of depression with any severity (Supplementary Fig 10).

Discussion

Depression Among HF Patients

With the technological advancement in chronic disease management, depression has been regarded as an important risk factor in increasing the burden of HF. The aim of the present meta-analysis study to investigate the prevalence of depression among HF patients. According to the best knowledge of the researchers, this is the first article to examine depression among HF patients for 20 years. In the final stage, 149 studies were performed on 305,407 HF patients. Unlike the previous study by Rutledge (2006), 21 studies entered the final stage.[2] The most commonly

used instruments included PHQ and BDI, which was consistent with the present systematic review and meta-analysis.[13]

The results showed that the global prevalence of any severity and moderate to severe severity of depression was 41.9% and 28.1%, respectively. Unlike the previous meta-analysis study in 2006, which was 21.5%.[2] This indicates that the prevalence of depression among HF patients has been increasing in recent years, which can be due to the larger number of studies included in the present study and the difference in the sample size of the studies included. The high prevalence of depression among HF patients can be because this phenomenon is often less considered and measured, which results in adverse clinical consequences such as increased mortality, increased length of hospital stay, and also increased costs imposed on the family and the health system.[6,14-16]

Consistent with the present study, in a previous systematic review performed on HF patients using implantable cardioverter defibrillator (ICD), Rio Huffman, J, showed that the prevalence of depression was between 11% and 28%.[17] Also, the prevalence of depression in the present study was consistent with studies performed on other heart patients including MI (28.7%),[18] and blood pressure (26.8%).[19] This may be due to the similar chronic nature of the diseases in them. However, the same figure was 25% in the general population[20] which is less than the present study.

The X Lin's meta-analysis study showed that the prevalence of depression among HF patients in China is 43%[21] and was higher than the present study. This could be due to the difference in the aim of X Lin's study and the present study. Also, studies conducted in all countries were included in the present study, but in another study, only studies conducted in China were included. This difference can also be due to the existence of different rehabilitation programs for heart patients to reduce depression in other countries. The prevalence of depression in women is about 1.5 times more than in men, which was consistent with previous studies.[21,2,7] The higher prevalence of depression in women can be due to certain psychological and emotional characteristics and how women adapt to depression, as well as more work stress. Another cause of more depression in women can be due to hormonal changes in them.[22,23]

The results also showed that the prevalence of depression in countries with low economic income (56.7%) is higher than in high-income countries (39.2%). We found no study in this regard, but evidence suggests that socioeconomic status is directly related to cardiovascular disease so that people are at lower risk of cardiovascular diseases in countries with better income status.[24,25]

The results of the present study also showed that the prevalence of depression HF patients in stages III and IV is higher than those in stages I and II, which was consistent with the previous studies carried out on heart patients.[21,2] The higher prevalence of depression in patients in stages III and IV can be due to the severity of the disease, exacerbation of symptoms, and inability of the patient to perform daily tasks.

Limitations and Strengths

The most important limitations of the present study included: One of the important limitations of the present study was the high heterogeneity among the studies, which could be due to differences in methods and instruments used for measuring depression in the studies, the cut-off point for calculating depression in different instruments, gender, age, and disease severity. Most of the studies were descriptive and had high heterogeneity. To reduce heterogeneity, the variables were classified according to subgroups. Since most of the studies were descriptive, the specific limitations of these studies should be considered when interpreting the data. The author was contacted for studies that did not provide complete information. To measure depression, various self-report and clinical instruments have been used that may affect the severity and prevalence of depression.

According to the best knowledge of the researchers, this is the first study that examines the prevalence of depression among HF patients over a long period. The standard Preferred Reporting Items for Systematic Reviews and Meta-Analyses method was used for this study. The study also examined the prevalence of depression based on WHO geographical areas and patients' economic status.

Conclusion

The present systematic review and meta-analysis were performed to evaluate the prevalence of depression among HF patients. The high prevalence of depression indicates the need to more attention to accurate and periodic measurement of depression among HF patients, holding training courses on a solution to prevent depression, especially in outpatient clinics. Also, due to the higher prevalence of depression in women and in patients with severe cardiac classes, there is a need to take into account comprehensive prevention programs for women and patients in the later stages of heart failure.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cpcardiol.2021.100848.

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